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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,319	03/21/2001	Ming-Hui Wei	CL001066-CIP	1556

7590 03/23/2004

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EXAMINER
BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,319	WEI ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,8,9 and 24-30* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,8,9 and 25-30* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

Applicant's election without traverse of Group IV, claims 4,5,8,9,22 and 23 in the election received 12/31/2003 is acknowledged. Applicant noted that claims 1-5 and 20-23 were omitted from the restriction requirement. Claims 1-5 and 20-23 are linking claims as set forth on pages 11-12 of the restriction requirement mailed 10/03/2003. Claims 4,5,22 and 23 link Groups II-IV and VI. Therefore, claims 4,5,8,9,22 and 23 are included in Group IV. Applicant has cancelled claims 1-3,5-7,10-23 and has added claims 24-30. Therefore, claims 4,8,9 and 24-30 are pending and under consideration in the instant office action.

Newly submitted claim 24 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 24 is drawn to a method of producing a polypeptide, which is patentably distinct from the elected invention of Claims 8 and 9, drawn to a nucleic acid that encodes the amino acid sequence shown in SEQ ID NO:2, an allelic variant of an amino acid sequence shown in SEQ ID NO:2 and cells comprising said nucleic acid. The polypeptide of the newly added claim does not require the nucleic acid of the elected invention and the nucleic acid does not require the polypeptide. The nucleic acid and the protein have distinct uses as well. The nucleic acid can be used as a probe while the protein can be used to generate antibody. Accordingly, claim 24 is withdrawn from consideration as being directed to a non-elected invention.

Priority

The first line of the specification claims priority as a Continuation In Part of US Patent

Application 09/752820, which has been abandoned. The current status of all nonprovisional parent applications referenced should be updated.

Claim Objections

Claim 4 is objected to because of the following informalities: Claim 4 is ended with a period at the end of section (c), however, there is a section (d) following (c). Furthermore, section (b) ends with "; and", which indicated the section (c) is the end of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4,8,9 and 25-30 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to an isolated nucleic acid consisting of SEQ ID NO:1 or 3 or the complement thereof or a nucleic acid encoding SEQ ID NO:2. Claim 9 is directed a host cell containing said nucleic acids.

The claimed invention is directed to a nucleotide sequence that encodes a novel human phosphatase. The instant specification has contemplated that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a human phosphatase based on its homology with other human phosphatases (page 6, lines 20-25). The specification asserts that, based on sequence homology, the claimed nucleic acid encodes a polypeptide with phosphatase activity and belongs to the PPM1G phosphatase subfamily and is a splice variant lacking exons 5-7 of PP2C-gamma (also called PPM1G). The specification has provided numerous general assertions and speculative uses for the claimed nucleic acids and cells comprising the claimed nucleic acids including use as probes, primers, chemical intermediates and use in biological assays (page 34, lines 9-10). The specification asserts that the nucleic acids can be used in diagnostic assays for qualitative changes in phosphatase nucleic acid expression that leads to pathology (page 38, lines 9-11). The specification asserts that the claimed nucleic acids can be used to detect mutations in the phosphatase gene that correlates to the claimed nucleic acid.

However, the specification fails to provide a specific and substantial utility for the claimed nucleotide sequences or the polypeptide that they encode. The evidence of record fails to set forth the substrate or the enzymatic product of the enzyme encoded by the claimed nucleic acid. The specification fails to demonstrate that mutations exist in the gene comprising the claimed nucleic acid or that the gene correlates with a disease. The asserted utilities provided by the specification are not specific to the nucleic acids encoding the phosphatase of the instant invention or even to phosphatases in general, but apply to any isolated nucleic acid.

The evidence of record fails even to correlate other members of the PPM1G phosphatase subfamily with any disease. Although the specification has contemplated that the detection of

mutated forms of the claimed sequences may be used as a diagnostic tool for an active disease (page 38, lines 19-21), no evidence has been presented that relates the claimed sequences to any disease.

A substantial utility is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities under §101. Applicant's specification fails to provide a "real world" use of the nucleic acids set forth in SEQ ID NO:1 or 3 or of any nucleic acid that encodes the polypeptide set forth in SEQ ID NO: 2. Neither the specification as filed, nor any art of record disclose or suggest any biological or biochemical activity for the protein encoded by SEQ ID NO: 1 or 3 or any nucleic acid encoding the polypeptide set forth by SEQ ID NO:2, such that any utility would be well established for the protein. The asserted utilities for the claimed nucleic acids such as a probe for diagnosing a disease, primers for PCR, or chemical intermediates is merely a "potential" use that applies to any uncharacterized, unrelated polynucleotide sequences. Therefore the asserted utilities are not considered "specific" utilities, i.e. they are not specific to SEQ ID NO:1,2 or 3.

The asserted utility of SEQ ID NO:1-3 is based on the assertion that SEQ ID NO:1 is a splice variant of the gene encoding PPM1G, which has phosphatase activity involved in spliceosome assembly (page 4, lines 20-30). The specification has not provided any evidence that the claimed nucleic acids, which lack exons 5-7 of PPM1G, encode a polypeptide with similar activity. The specification has failed to provide evidence of any structural elements, that are related to phosphatases in general or specific to PPM1G, that may be present within the claimed sequence to support such assertions. In any event, assuming the assertions of the instant

specification are correct and that SEQ ID NO: 2 encodes a phosphatase of some kind, it is unclear exactly which type of phosphatase is encoded by the claimed sequence, or what substrates the putative phosphatase acts on and what type of cellular process it affects. The PPM1G subfamily of phosphatases has no demonstrated link to any disease. The general class of phosphatases is comprised of many members, which have different chemical structures, different tissue specificities, different activators and inhibitors, and more importantly, different substrates. The specification (see pages 1-4) and the state of the art teaches the variability in function of known phosphatases as regulators of processes as diverse as cell growth, differentiation, cell-to cell contacts, cell cycle progression and oncogenesis. For example, Li (2000, Seminars in Immunology, Vol. 12, pages 75-84) taught that a specific family of phosphatases, protein tyrosine phosphatases (PTPs), are crucial for regulation of numerous cellular events including cell growth, differentiation and communication. The PTPs are so diverse within their subfamily of phosphatases that some are localized to the cell membrane while others act in the cytosol. Membrane localized PTPs, can be further subdivided into 5 types based on their extracellular domain. Knockout of various mouse PTPs lead to a variety of unrelated phenotypes including hematopoietic hyperproliferation, lymphocyte abnormalities, increased neonatal death, stunted growth and impaired mammary development (page 81, column 2). Various PTPs also correlate with a vast array of diseases in humans including Lafora's disease (characterized by seizures) and cancer (page 81, col. 1, last paragraph-page 82 column 2, last paragraph). Furthermore, Ceulemans highlights a property of a number of phosphatase in that Protein Phosphatase-1 has numerous roles by acting on numerous substrates (2004, Physiol. Rev., Vol/ 84, pages 1-39, see for example, page 1).

These references demonstrate the biochemical diversity between phosphatase family members and their differing roles in various cell processes. Neither the specification nor any art of record has taught the activity of the phosphatase set forth by SEQ ID NO:2 leaving the skilled artisan to speculate and investigate the uses of the uncharacterized phosphatase. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed nucleic acids and the protein they encode. In view of the lack of guidance with respect to the activity of the phosphatase the claimed invention encompasses or its role in the cell, the skilled artisan would not know how to use the claimed nucleotide sequence or its expression product. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Claims 4,8,9 and 25-30 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 9 is further not enabled under 35 U.S.C. 112, first paragraph. Claim 9 is drawn to a host cell containing the nucleic acid of claim 4 and encompasses cells in vivo as well as in vitro. While enabling for an isolated host cell in vitro, the specification is not enabling for host cells in vivo and their use in gene therapy as broadly encompassed by the claim. The specification provides general and prophetic teachings regarding use of the claimed cells for ex vivo gene therapy (page 41, lines 17-21). The specification fails to provide any teachings with respect to

gene therapy that are specific to the claimed cells. The specification does not teach what diseases, what cell types, what vectors or what means of delivery of the cells should be used to treat a disease using the claimed cells.

The nature of the invention being gene therapy, the state of the prior art is not well developed and is highly unpredictable. Verma (1997, Nature, Vol. 389, pages 239-242) states that out of the more than 200 clinical trials currently underway, no single outcome can be pointed to as a success story (page 239, col. 1). Numerous factors complicate the gene therapy art that have not been overcome by routine experimentation. Eck and Wilson explain that the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced are all factors that differ dramatically based on the vector used, the protein being produced, and the disease being treated (Eck and Wilson, 1996, 'Gene-Based Therapy' in The Pharmacological Basis of Therapeutics, paragraph bridging pages 81-82). Verma states that one major obstacle to success has been the inability to deliver genes efficiently and obtain sustained expression (page 239, column 3). It is further noted that Eck and Wilson support the importance of tailoring a gene therapy vector and methods to specific diseases and disorders (see page 82, column 1, 1st paragraph). For example, Eck and Wilson review the state of the art for gene therapy for inherited disorders and disclose that "the level of protein function necessary to achieve

complementation of the defect varies among genetic diseases (see page 78, column 2, 2nd paragraph).

The instant specification does not provide any *in vivo* working examples and teaches only prophetically that the claimed cells can be used to treat disease. The specification does not provide any correlation between the gene encoding the claimed phosphatase and any disease to be treated. The specification does not teach how to construct an effective therapeutic vector, how to deliver it such that it a therapeutic level of expression can be achieved to effect a therapeutic response to any particular disease in any particular tissue. Given the lack of guidance in the specification, one of skill would not know what disease to treat using the claimed cells or how to treat a disease using the claimed nucleic acid. As such, in light of the lack of guidance provided by the specification and the unpredictable nature of the gene therapy art, it would require undue experimentation to use the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Fri 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PETER PARAS, JR.
PRIMARY EXAMINER

Valarie Bertoglio
Examiner
Art Unit 1632